

In the claims:

Please amend the claims as follows:

---

1. (Cancel) A method for screening compounds inhibiting signal transduction through inflammatory cytokines, the method comprising the steps of:
  - (a) contacting a test sample with TAK1 and TAB1;
  - (b) detecting binding between the TAK1 and the TAB1; and
  - (c) selecting a compound inhibiting the binding.
2. (Currently amended) The method of claim + 41, wherein the TAK1 and/or the TAB1 is fused with a peptide.
3. (Currently amended) The method of claim + 41, wherein the TAK1 or the TAB1 is linked to a support.  
*B1*
4. (Currently amended) The method of claim + 41, wherein a label is attached to the TAK1 or the TAB1 and wherein the binding is detected by detecting or measuring the label.
5. (Currently amended) The method of claim + 41, wherein the binding is detected by detecting or measuring the TAB1 bound to the TAK1 with a primary antibody against TAB1 or a primary antibody against ~~the~~ a peptide fused with the TAB1.
6. (Currently amended) The method of claim + 41, wherein the binding is detected by detecting or measuring the TAK1 bound to the TAB1 with a primary antibody against TAK1 or a primary antibody against ~~the~~ a peptide fused with the TAK1.
7. (Currently amended) The method of claim + 41, wherein the binding is detected by detecting or measuring the TAB1 bound to the TAK1 with a primary antibody against the TAB1 or a primary antibody against ~~the~~ a peptide fused with TAB1, and a secondary antibody against the primary antibody.

8. (Currently amended) The method of claim + 41, wherein the binding is detected by detecting or measuring the TAK1 bound to the TAB1 with a primary antibody against TAK1 or a primary antibody against ~~the~~ a peptide fused with the TAK1, and a secondary antibody against the primary antibody.

9. (Currently amended) The method of claim 5 7, wherein the primary antibody or the secondary antibody is labeled with a radioisotope, enzyme, or fluorescent substance.

10. (Currently amended) The method of claim 2, wherein the binding is detected ~~with, as an index; as a~~ change in the expression level of a reporter gene which is activated in response to the binding.

11. (Currently amended) The method of claim 10, wherein the reporter gene is encodes luciferase, chloramphenicol acetyltransferase, green fluorescent protein, or  $\beta$ -galactosidase.

12-26. (Withdrawn)

27. (Currently amended) The method of claim + 41, wherein the inflammatory cytokine is IL-1, TNF, IL-10, or IL-6.

41. (New) A screening method comprising:  
(a) providing a sample comprising a TAK1 and a TAB1;  
(b) contacting the sample with a compound;  
(c) detecting binding between the TAK1 and the TAB1;  
(d) selecting the compound if binding between the TAK1 and TAB1 is inhibited in the sample compared to a control; and

(c) testing the selected compound to determine whether it inhibits expression of an inflammatory cytokine in a cell or cell-free system that comprises a TAK1, a TAB1, and a gene encoding the inflammatory cytokine,

wherein the TAK1 of (a) is selected from the group consisting of

(i) a protein comprising amino acids 76 to 303 of SEQ ID NO:2;

(ii) a protein that binds to the TAB1 of (a) and comprises amino acids 76-303 of SEQ ID NO:2, with one to twenty amino acids substituted, deleted, and/or added; and

(iii) a protein that binds to the TAB1 of (a) and comprises an amino acid sequence encoded by a DNA sequence that hybridizes with the complement of nucleotides 408 to 1091 of SEQ ID NO:1 under washing conditions of 42°C, 5 x SSC, 0.1% sodium dodecyl sulfate, and 50% formamide; and

wherein the TAB1 of (a) is selected from the group consisting of

(iv) a protein comprising amino acids 437 to 504 of SEQ ID NO:4;

(v) a protein that binds to the TAK1 of (a) and comprises amino acids 437-504 of SEQ ID NO:4, with one to twenty amino acids substituted, deleted, and/or added; and

(vi) a protein that binds to the TAK1 of (a) and comprises an amino acid sequence encoded by a DNA that hybridizes with the complement of nucleotides 1338 to 1541 of SEQ ID NO:3 under washing conditions of 42°C, 5 x SSC, 0.1% sodium dodecyl sulfate, and 50% formamide.

42. (New) The method of claim 41, wherein the TAK1 of (a) comprises amino acids 76 to 303 of SEQ ID NO:2.

43. (New) The method of claim 41, wherein the TAK1 of (a) is a protein that binds to the TAB1 of (a) and comprises amino acids 76-303 of SEQ ID NO:2, with one to twenty substitutions, deletions, and/or additions.

44. (New) The method of claim 41, wherein the TAB1 of (a) is a protein that binds to the TAB1 of (a) and comprises amino acids 76-303 of SEQ ID NO:2, with one to ten substitutions, deletions, and/or additions.

45. (New) The method of claim 41, wherein the TAB1 of (a) is a protein that binds to the TAB1 of (a) and comprises amino acids 76-303 of SEQ ID NO:2, with one or two substitutions, deletions, and/or additions.

46. (New) The method of claim 41, wherein the TAB1 of (a) is a protein that binds to the TAB1 of (a) and comprises an amino acid sequence encoded by a DNA that hybridizes with the complement of nucleotides 408 to 1091 of SEQ ID NO:1 under washing conditions of 42°C, 5 x SSC, 0.1% sodium dodecyl sulfate, and 50% formamide.

47. (New) The method of claim 41, wherein the TAB1 of (a) is a protein that binds to the TAB1 of (a) and comprises an amino acid sequence that is encoded by a DNA that hybridizes with the complement of nucleotides 408 to 1091 of SEQ ID NO:1 under washing conditions of 60°C, 0.1 x SSC, and 0.1% sodium dodecyl sulfate.

48. (New) The method of claim 41, wherein the TAB1 of (a) comprises the amino acids 437 to 504 of SEQ ID NO:4.

49. (New) The method of claim 41, wherein the TAB1 of (a) is a protein that binds to the TAB1 of (a) and comprises amino acids 437-504 of SEQ ID NO:4, with one to twenty amino acids substituted, deleted, and/or added.

50. (New) The method of claim 41, wherein the TAB1 of (a) is a protein that binds to the TAB1 of (a) and comprises amino acids 437-504 of SEQ ID NO:4, with one to ten amino acids substituted, deleted, and/or added.

51. (New) The method of claim 41, wherein the TAB1 of (a) is a protein that binds to the TAK1 of (a) and comprises amino acids 437-504 of SEQ ID NO:4, with one or two amino acids substituted, deleted, and/or added.

52. (New) The method of claim 41, wherein the TAB1 of (a) is a protein that binds to the TAK1 of (a) and comprises an amino acid sequence encoded by a DNA that hybridizes with the complement of nucleotides 1338 to 1541 of SEQ ID NO:3 under washing conditions of 42°C, 5 x SSC, 0.1% sodium dodecyl sulfate, and 50% formamide.

53. (New) The method of claim 41, wherein the TAB1 of (a) is a protein that binds to the TAK1 of (a) and comprises an amino acid sequence encoded by a DNA that hybridizes with the complement of nucleotides 1338 to 1541 of SEQ ID NO:3 under washing conditions of 60°C, 0.1 x SSC, and 0.1% sodium dodecyl sulfate.

54. (New) The method of claim 41, wherein the inflammatory cytokine is IL-1.

55. (New) The method of claim 41, wherein the inflammatory cytokine is TNF.

56. (New) The method of claim 41, wherein the inflammatory cytokine is IL-6.

57. (New) The method of claim 41, wherein the inflammatory cytokine is IL-10.

58. (New) The method of claim 41, wherein step (e) comprises contacting the cell or cell-free system with a substance that induces inflammation.

59. (New) The method of claim 58, wherein the substance is a lipopolysaccharide or an inflammatory cytokine.

60. (New) The method of claim 58, wherein the substance is IL-1 or TNF.

61. (New) A screening method comprising

- (a) identifying a compound as an inhibitor of inflammatory cytokine activity;
- (b) providing a sample comprising a TAK1 and a TAB1;
- (c) contacting the sample with the compound;
- (d) detecting binding between the TAK1 and the TAB1; and
- (e) selecting the compound if binding between the TAK1 and TAB1 is inhibited in the sample compared to a control,  
wherein the TAK1 is selected from the group consisting of
  - (i) a protein comprising amino acids 76 to 303 of SEQ ID NO:2;
  - (ii) a protein that binds to the TAB1 and comprises amino acids 76-303 of SEQ ID NO:2, with one to twenty amino acids substituted, deleted, and/or added;  
and
  - (iii) a protein that binds to the TAB1 and comprises an amino acid sequence encoded by a DNA sequence that hybridizes with the complement of nucleotides 408 to 1091 of SEQ ID NO:1 under washing conditions of 42°C, 5 x SSC, 0.1% sodium dodecyl sulfate, and 50% formamide; and  
wherein the TAB1 is selected from the group consisting of
    - (iv) a protein comprising amino acids 437 to 504 of SEQ ID NO:4;
    - (v) a protein that binds to the TAK1 and comprises amino acids 437-504 of SEQ ID NO:4, with one to twenty amino acids substituted, deleted, and/or added;  
and
    - (vi) a protein that binds to the TAK1 and comprises an amino acid sequence encoded by a DNA that hybridizes with the complement of nucleotides 1338 to 1541 of SEQ ID NO:3 under washing conditions of 42°C, 5 x SSC, 0.1% sodium dodecyl sulfate, and 50% formamide.

62. (New) The method of claim 61, wherein the inflammatory cytokine is TNF, IL-6, or IL-10.

63. (New) A screening method comprising

- (a) providing a sample comprising a TAK1 and a TAB1;
- (b) contacting the sample with a compound;
- (c) detecting binding between the TAK1 and the TAB1;
- (d) selecting the compound if binding between the TAK1 and TAB1 is inhibited in

the sample compared to a control; and

- (e) testing whether the selected compound inhibits
  - (i) inflammation in an animal, or
  - (ii) inflammatory cytokine expression in an animal,

wherein the TAK1 is selected from the group consisting of

- (1) a protein comprising amino acids 76 to 303 of SEQ ID NO:2;
- (2) a protein that binds to the TAB1 and comprises amino acids 76-303 of SEQ ID NO:2, with one to twenty amino acids substituted, deleted, and/or added; and
- (3) a protein that binds to the TAB1 and comprises an amino acid sequence encoded by a DNA sequence that hybridizes with the complement of nucleotides 408 to 1091 of SEQ ID NO:1 under washing conditions of 42°C, 5 x SSC, 0.1% sodium dodecyl sulfate, and 50% formamide; and

wherein the TAB1 is selected from the group consisting of

- (4) a protein comprising amino acids 437 to 504 of SEQ ID NO:4;
- (5) a protein that binds to the TAK1 and comprises amino acids 437-504 of SEQ ID NO:4, with one to twenty amino acids substituted, deleted, and/or added; and
- (6) a protein that binds to the TAK1 and comprises an amino acid sequence encoded by a DNA that hybridizes with the complement of nucleotides 1338 to 1541 of SEQ ID NO:3 under washing conditions of 42°C, 5 x SSC, 0.1% sodium dodecyl sulfate, and 50% formamide.

64. (New) The method of claim 63, wherein step (e) comprises administering to the animal a lipopolysaccharide or an inflammatory cytokine.

65. (New) The method of claim 63, wherein the inflammatory cytokine is IL-1, TNF, IL-6, or IL-10.

66. (New) The method of claim 64, wherein the inflammatory cytokine administered to the animal is IL-1 or TNF.

67. (New) A screening method comprising:

- (a) providing a sample comprising a TAK1 and a TAB1;
- (b) contacting the sample with a compound;
- (c) detecting binding between the TAK1 and the TAB1;
- (d) selecting the compound if binding between the TAK1 and TAB1 is inhibited in

the sample compared to a control; and

(e) identifying the selected compound as an inhibitor of inflammatory cytokine activity,

wherein the TAK1 of (a) is selected from the group consisting of

- (i) a protein comprising amino acids 76 to 303 of SEQ ID NO:2;
- (ii) a protein that binds to the TAB1 of (a) and comprises amino acids 76-303 of SEQ ID NO:2, with one to twenty amino acids substituted, deleted, and/or added; and
- (iii) a protein that binds to the TAB1 of (a) and comprises an amino acid sequence encoded by a DNA sequence that hybridizes with the complement of nucleotides 408 to 1091 of SEQ ID NO:1 under washing conditions of 42°C, 5 x SSC, 0.1% sodium dodecyl sulfate, and 50% formamide; and

wherein the TAB1 of (a) is selected from the group consisting of

- (iv) a protein comprising amino acids 437 to 504 of SEQ ID NO:4;
- (v) a protein that binds to the TAK1 of (a) and comprises amino acids 437-504 of SEQ ID NO:4, with one to twenty amino acids substituted, deleted, and/or added; and
- (vi) a protein that binds to the TAK1 of (a) and comprises an amino acid sequence encoded by a DNA that hybridizes with the complement of nucleotides 1338 to 1541 of SEQ ID NO:3 under washing conditions of 42°C, 5 x SSC, 0.1% sodium dodecyl sulfate, and 50% formamide.